

WHAT IS CLAIMED IS:

1. An isolated and purified DNA molecule comprising at least one DNA segment, a biologically active subunit or variant thereof, of a circular intermediate of adeno-associated virus, which DNA segment confers increased episomal stability, persistence or abundance of the isolated DNA molecule in a host cell.
2. The DNA molecule of claim 1 in which the DNA segment comprises at least a portion of a 5' inverted terminal repeat of adeno-associated virus.
3. The DNA molecule of claim 1 in which the DNA segment comprises at least a portion of a 3'-inverted terminal repeat of adeno-associated virus.
4. The DNA molecule of claim 1 which further comprises a marker or selectable gene.
5. A plasmid comprising the DNA molecule of claim 1.
6. A gene transfer vector, comprising:
 - a) at least one first DNA segment, a biologically active subunit or variant thereof, of a circular intermediate of adeno-associated virus, which DNA segment confers increased episomal stability or integration of the vector in a host cell; and
 - b) a second DNA segment comprising a gene.
7. The vector of claim 6 in which the first DNA segment comprises at least about 550 bp of adeno-associated virus sequence.

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8. The vector of claim 6 in which the first DNA segment comprises at least about 400 bp of adeno-associated virus sequence.

9. A therapeutic gene transfer vector, comprising:

- at least one first DNA segment, a biologically active subunit or variant thereof, of a circular intermediate of adeno-associated virus, which DNA segment confers increased episomal stability or integration of the vector in a host cell; and
- a second DNA segment comprising a gene encoding a therapeutically effective polypeptide.

10. A method of delivering a gene to a cell comprising: contacting the cell with the vector of claim 6 or 9.

11. A composition for delivering a gene to a cell, comprising: the vector of claim 6 or 9 and a delivery vehicle.

12. The composition of claim 11 wherein the delivery vehicle is a pharmaceutically acceptable carrier.

13. The composition of claim 11 wherein the delivery vehicle is a liposome.

14. The DNA molecule of claim 1 which comprises concatamers of the circular intermediate.

15. The DNA molecule of claim 1 in which the stability, persistence or abundance of the DNA in cells is enhanced by a DNA binding protein.

16. The DNA molecule of claim 15 wherein the DNA binding protein is adenovirus E2a.

17. A host cell comprising the vector of claim 6 or 9.

18. A host cell comprising the DNA molecule of claim 1.

19. An animal comprising the vector of claim 6 or 9.

20. The animal of claim 19 which is not a human.

21. A method of expressing a gene product in the muscle tissue of an animal, which comprises: administering the vector of claim 6 or 9 to the muscle tissue of said animal in an amount effective to express the gene.

22. The method of claim 21 wherein the vector is administered dissolved or suspended in a liquid pharmaceutically acceptable carrier. *B*

23. The method of claim 22 wherein said liquid carrier comprises an aqueous solution.

24. The method of claim 21 wherein said gene comprises a DNA segment encoding a protein operably linked to a promoter operable in said muscle tissue.

25. The method of claim 21 wherein said administering is by intramuscular injection.

26. The method of claim 21 wherein said administering is by transdermal transport.

27. The method of claim 21 wherein said animal is a bird or mammal.

28. The method of claim 1 wherein said animal is a human.

29. A method of expressing a gene in a eukaryotic cell, comprising:
a) transfecting a eukaryotic host cell susceptible to adenovirus infection with the vector of claim 6 or 9 and a recombinant adenovirus helper vector so as to form packaged viral particles; and
b) infecting a eukaryotic host cell with the viral particles in an amount effective to detect expression of the gene.

30. A composition comprising:
a) a first adeno-associated virus vector comprising linked:
i) a first DNA segment comprising a 5'-inverted terminal repeat of adeno-associated virus;
ii) a second DNA segment comprising at least a portion of an open reading frame operably linked to a promoter, wherein the DNA segment does not comprise the entire open reading frame;
iii) a third DNA segment comprising a splice donor site; and
iv) a fourth DNA segment comprising a 3'-inverted terminal repeat of adeno-associated virus; and
b) a second adeno-associated virus vector comprising linked:
i) a first DNA segment comprising a 5'-inverted terminal repeat of adeno-associated virus;
ii) a second DNA segment comprising a splice acceptor site;
iii) a third DNA segment comprising at least a portion of an open reading frame which together with the DNA segment

of (a)(ii) encodes a full-length polypeptide;
and

iv) a fourth DNA segment comprising a β' -inverted terminal repeat of adeno-associated virus.

31. The composition of claim 30 further comprising a delivery vehicle.

32. A method to transfer and express a polypeptide in a host cell comprising contacting the host cell with the composition of claim 30.

33. A method to transfer and express a polypeptide in a host cell comprising contacting the host cell with a first adeno-associated virus vector comprising linked:

- i) a first DNA segment comprising a 5'-inverted terminal repeat of adeno-associated virus;
- ii) a second DNA segment comprising at least a portion of an open reading frame operably linked to a promoter, wherein the DNA segment does not comprise the entire open reading frame;
- iii) a third DNA segment comprising a splice donor site; and
- iv) a fourth DNA segment comprising a 3'-inverted terminal repeat of adeno-associated virus.

34. The method of claim 33 wherein the host cell is further contacted with a second adeno-associated virus vector comprising linked:

- i) a first DNA segment comprising a 5'-inverted terminal repeat of adeno-associated virus;
- ii) a second DNA segment comprising a splice acceptor site;

- iii) a third DNA segment comprising at least a portion of an open reading frame which together with the DNA segment of (a)(ii) encodes a full-length polypeptide;
and
- iv) a fourth DNA segment comprising a 3'-inverted terminal repeat of adeno-associated virus.

35. The method of claim 32 or 33 wherein the host cell is a lung epithelial cell, a muscle cell or a neuron.

36. The method of claim 32 or 34 wherein the polypeptide is the CFTR polypeptide.

37. A method of expressing a gene product in the muscle tissue of an animal, comprising contacting the muscle tissue with the composition of claim 30 in an amount effective to express the polypeptide.

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38. A method of expressing a gene product in the airway epithelia of an animal, comprising contacting the airway epithelia with the composition of claim 30 in an amount effective to express the polypeptide.

39. A method of expressing a gene product in the neurons of an animal, comprising contacting the neurons with the composition of claim 30 in an amount effective to express the polypeptide.

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